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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,394	12/11/2001	Kevin P. Baker	39780-2830P1C41	9887

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,394	BAKER ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SUPPLEMENTAL DETAILED ACTION

Upon further consideration, a supplemental action on the claims follows below. It is noted that the references cited by the Examiner were made of record on the PTO-892 mailed 10 August 2004.

Status of Application, Amendments and/or Claims

The amendments of 11 April 2003, 09 September 2002, and 11 December 2001 have been entered in full. Claims 1-27 are cancelled and claims 28-33 are added.

Claims 28-33 are under consideration in the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 13 November 2002 has been considered by the examiner and was made of record in the Action mailed 10 August 2004. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Priority

Applicant's claim for priority under 35 U.S.C. 120 and 119(e) is acknowledged. The instant application claims priority to 09/946, 374 (9/4/2001), PCT/US000/04342 (2/18/2000), 09/403,297 (10/18/1999), PCT/US99/2011 (9/1/1999), and 60/108,787 (11/17/1998). The polynucleotide of SEQ ID NO: 375 and the polypeptide of SEQ ID NO: 376 of the instant application are fully disclosed in the prior applications.

Specification

1. The disclosure is objected to because of the following informalities:

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (See pg 304, line 5; pg 306, line 23, for example). Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "ANTIBODY THAT BINDS A SECRETED POLYPEPTIDE".

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 28, 31, 33 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The claims read on a product of nature in that the claimed antibody is not "isolated". For example, the claims encompass polyclonal sera that has not been removed from the human or animal. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter: See *Diamond v. Chakrabarty,*

447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified". See MPEP 2105.

5. Claims 28-33 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

Specifically, claims 28-33 are directed to an antibody that binds to the polypeptide shown in Figure 220 (SEQ ID NO: 376). The claims also recite that the antibody is monoclonal or humanized. The claims recite that the antibody is an antibody fragment or that the antibody is labeled. The claims recite that the antibody specifically binds to the polypeptide shown in Figure 220 (SEQ ID NO: 376). However, the instant specification does not teach any significance or functional characteristics of the PRO1760 polypeptide (SEQ ID NO: 376) or antibody. The specification also does not disclose any specific methods or working examples for the production of the antibody or labeling of the antibody. Since the utility is not presented in mature form and significant further research is required, the utility is not substantial. The specification asserts the following as patentable utilities for the claimed putative antibody against PRO1760 (SEQ ID NO: 376):

1) to detect PRO1760 polypeptide expression in specific cells, tissues, or serum (pg 380, lines 1-13)

2) as a therapeutic for treatment of various disorders (pg 379, lines 1-3)

3) for purification of PRO1760 from recombinant cell culture or natural sources (pg 380, lines 15-16)

Each of these shall be addressed in turn.

1) to detect PRO1760 polypeptide expression in specific cells, tissues, or serum. This asserted utility is not specific or substantial. Such assays can be performed with any antibody. Further, the specification discloses nothing specific or substantial for the PRO1760 polypeptide detected by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) as a therapeutic for treatment of various disorders. This asserted utility is not specific or substantial. Such assays can be performed with any antibody. The specification discloses nothing about the normal level of expression of the PRO1760 polypeptide. The specification does not disclose any disorders which are associated with altered levels or forms of the PRO1760 polypeptide. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) for purification of PRO1760 from recombinant cell culture or natural sources. This asserted utility is not specific or substantial. Such assays can be performed with any antibody. Further, the specification discloses nothing specific or substantial for the PRO1760 polypeptide purified by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6. Claims 28-33 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a

well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. It is noted to Applicant that Examples 149 and 154 on pages 511 and 514 of the specification, respectively, also do not provide any activity of the PRO1760 antibody to establish a credible, specific, and substantial asserted utility or a well established utility or enablement. The asserted utility of Example 149, inhibition of glucose uptake by rat adipocytes, is not substantial. The specification teaches that "as the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay is greater than 1.5 times or less than 0.5 times the insulin control" (pg 512, lines 4-6). Although the specification teaches that PRO1760 is positive as an inhibitor in this assay, the specification does not disclose any specific resulting cell numbers or percentages, statistical differences, or the number of repetitions for the assay. Without this knowledge, which could not be gleaned from the instant specification, one of ordinary skill in the art at the time the invention was made would not have been able to use the information obtained from this assay in a useful manner. One skilled in the art would be unable to repeat the assay with a compound (such as one of the PRO1760 variants encompassed by the claims) and determine whether the compound scored positive or negative. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Furthermore, the specification of the instant application teaches that PRO polypeptides that inhibit glucose uptake by adipocytes would be beneficial for the therapeutic treatment of disorders including for example, obesity, diabetes, or hyper- or hypo-insulinemia (pg 511, lines 18-20). However, it is not clear how PRO1760, which inhibits glucose uptake as asserted by the specification, is

beneficial to such disorders because in these conditions little or no glucose is entering the cells to begin with. The cells are unable to utilize glucose. Therefore, why would one skilled in the art want to exacerbate this situation even more by the addition of PRO1760? Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, therefore both polypeptide and its antibodies have no patentable utility.

Furthermore, the asserted utility of Example 154, the inhibition of heart neonatal hypertrophy is not substantial. The specification teaches that "a positive in the assay occurs when the PRO polypeptide treated myocytes are visually smaller on the average or less numerous than the untreated myocytes" (pg 514, lines 33-34). Although the specification teaches that PRO1760 is positive in this assay, the specification does not disclose any specific resulting cell numbers, statistical differences, or the number of repetitions for the assay. For example, there is no indication in the specification as to statistically how much smaller the PRO polypeptide treated myocytes are as compared to control. Without this knowledge, which could not be gleaned from the instant specification, one of ordinary skill in the art at the time the invention was made would not have been able to use the information obtained from this assay in a useful manner. One skilled in the art would be unable to repeat the assay with a compound (such as one of the PRO1760 variants encompassed by the claims) and determine whether the compound scored positive or negative. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. Furthermore, PRO1760 may not necessarily inhibit the neonatal heart hypertrophy condition itself, but rather, simply bind LIF or ET-1, which are the factors utilized to induce the hypertrophy. The state of the art is also such that a rat cardiac myocyte cell culture is not an art

recognized model for heart hypertrophy, but instead is used to "explore the regulation of myocardial cell hypertrophy" (Simpson et al., Circ Res 51(6): 787-801, 1982; last sentence in abstract; Ueyama et al., J Mol Cell Cardiol 32: 947-960, 2000). Again, antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, therefore both polypeptide and its antibodies have no patentable utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 28-33 are rejected as being indefinite because the difference between "an antibody that binds to the polypeptide" as recited in claim 28 and "an antibody which specifically binds to the polypeptide" as recited in claim 33 cannot be determined, absent a definition of "specific binding". It is not clear what each claim is meant to encompass, given that neither the art nor the specification provide a clear definition for, or distinction between, "binds" and "specifically binds". Therefore, the metes and bounds of the claimed invention cannot be determined.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Ruben et al. U.S. Patent 6,475,753. (It is noted that the amino acid sequence of SEQ ID NO: 394 of Ruben has 100% sequence identity to the polypeptide of SEQ ID NO: 376 of the instant application. Although Ruben et al. claims priority to numerous provisional applications, SEQ ID NO: 394 could not be located in these applications. Therefore, the priority date of the polypeptide of SEQ ID NO: 394 is deemed to be 12/14/1999. The instant application fully discloses SEQ ID NO: 376 in the provisional application of 60/108,787 filed 11/17/1998.)

Clark et al. Genome Res 13(10) : 2265-2270, 2003 (review discussing the SDPI project).

Strausberg et al. Proc Natl Acad Sci USA 99(26): 16899-16903, 2002 (review of project to identify human and mouse genes).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
20 October 2004

Bridget E. Bunner